

EXHIBIT 8



National Institute of Neurological Disorders and Stroke

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Report on the Neuropathology of Chronic Traumatic Encephalopathy Workshop

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National Institutes of Health, Bethesda, Maryland

Sports and Health Research Program

On December 5-6, 2012, 60 scientists and clinicians attended a meeting at the National Institutes of Health (NIH) in Bethesda, Maryland to identify **what is known about chronic traumatic encephalopathy (CTE) neuropathology and what research strategies and resources can fill critical gaps in knowledge**. Organized by Walter Koroshetz, M.D., Deputy Director of the National Institute of Neurological Disorders and Stroke (NINDS); Dennis Dickson, M.D., Professor of Pathology, Mayo Clinic, Jacksonville; and Ramona Hicks, Ph.D., Traumatic Brain Injury Program Director at NINDS, the workshop brought together experts on CTE and Alzheimer's disease, as well as stakeholders from sports and military interests. The event was supported by the newly formed Sports and Health Research Program, a public-private partnership of the NIH, the Foundation for NIH, and the National Football League (NFL), aimed at addressing major public health issues related to sports participation and other activities involving repetitive head injuries. Among the key questions addressed were:

What do we know about the neuropathology of CTE?

In 1928, it was recognized that boxers with repetitive head injury developed dementia due to a unique brain degeneration characterized by neurons filled with tangles of a protein called tau as well as widespread loss of brain cells. More recently this disorder, initially termed "dementia pugilistica", has occurred in non-boxers exposed to varying degrees of repetitive head injury. Chronic traumatic encephalopathy (CTE) is the term currently used to describe this condition. CTE can only be confirmed by pathologic examination of brains from individuals who have died. Ann McKee, M.D., Co-Director of the Center for the Study of Traumatic Encephalopathy at Boston University School of Medicine, autopsied the brains of 85 men with a history of repetitive mild traumatic brain injury ([Brain 2012; doi: 10.1093/brain/aws307](#)). Her group described a spectrum of abnormalities in these brains, with the signature finding being the deposition of tau in neurons. Abnormal tau accumulation has been identified in brain tissue in several other neurodegenerative diseases, including Alzheimer's disease. Dr. Dickson noted that none of the individual pathologic features (such as tau pathology) are unique to CTE, but what confers uniqueness is their peculiar distribution within the brain. Dr. McKee proposed four clinically distinct stages of CTE pathology based on the location, pattern and extent of tau accumulation. Advanced stages of the brain pathology were generally observed in older individuals with a history of a progressive dementia and brain atrophy. In the more mildly

affected brains, tau pathology was clustered around small blood vessels in the depths of the brain's folds (sulci) and in the brain's superficial layers and atrophy was absent.

The symptoms of CTE appear to fall into at least two clearly distinguishable patterns, according to Robert Stern, Ph.D., Co-Director of the Center for the Study of Traumatic Encephalopathy at Boston University School of Medicine. His study found that younger people (ages 20-40) tended to have a rapid course of disease progression primarily involving behavioral and mood changes, whereas older people (ages 50-70) had a slower course of disease progression involving primarily cognitive difficulties leading to dementia. This raises the question as to whether there are two distinct pathological processes or a single process whose expression changes over time.

There also was discussion of brain alterations that occur over many years in persons who suffered a single, severe TBI. Postmortem brain studies in such individuals who survive for years after the injury suggest that pathological processes, including tau accumulation, continue long after the injury itself, according to William Stewart, Ph.D., Neuropathologist for the National Health Service of Greater Glasgow and Clyde.

What neuroimaging tools and biomarkers show promise in diagnosing CTE?

A major focus of the conference was how the pathological features of CTE identified at autopsy could be correlated with imaging studies of autopsied brains. If correlations could be determined, the neuroimaging techniques could then be tested for their ability to diagnose CTE in living persons. Diffusion tensor imaging (DTI), a type of magnetic resonance imaging (MRI) that reveals white matter tracts, shows promise for detecting CTE. Substantial technological improvements are needed before DTI is ready for routine clinical use, according to David Brody, M.D., Ph.D., Associate Professor of Neurology at Washington University School of Medicine. MRI studies also are complicated by the enormous amount of data collected, said Susumu Mori, Ph.D., Assistant Professor at Johns Hopkins University School of Medicine. Before DTI and other MRI techniques are applicable for assessing CTE in a living person, their accuracy and precision need to improve. Positron emission tomography, or PET scanning, is another imaging tool that shows promise for detecting CTE. PET scanning can map the location of particular molecules in the brain. Novel PET markers now are being validated to detect tau abnormalities associated with neurodegenerative disease, according to Hartmuth Kolb, Ph.D., Vice President of Biomarker Research at Siemens Healthcare. A PET marker that identifies the tau pathology of CTE in living individuals would constitute a major breakthrough in the field.

Who is at risk and what are the symptoms?

Currently a definitive diagnosis of CTE is only possible after death and the brains studied to date come from a highly selected population of mostly professional athletes. As a result, no data indicating the frequency of CTE are available. Similarly, we do not understand which individuals with multiple impacts to the head, as those that occur commonly in children and adults engaged in contact sports, are at risk for CTE. Athletes playing competitive football over the course of high school and college, for example, are estimated to suffer upwards of 8,000 hits to the head according to Thomas McAllister,

M.D., Vice Chair for Neuroscience Research at the Geisel School of Medicine at Dartmouth. To gain a better understanding of the relationship between the number and intensity of these hits on brain function, Dr. McAllister's research team placed force-sensors inside the helmets of college football players. They discovered that while some athletes develop concussions following very low-impact hits, others do not, even after sustaining harder hits. They also discovered that as a group the players were not found to have cognitive differences before and after one football season.

Research in the field of biomarkers for TBI and Alzheimer's disease has advanced rapidly in the last two decades, according to Linda Papa, M.D., Director of Academic Clinical Research at the Orlando Regional Medical Center. Although biomarkers in the blood demonstrate potential for guiding medical management of patients with mild to moderate TBI in the emergency department, very few studies have looked at biomarkers that address the long-term disease processes of CTE. Much work remains to identify useful, validated biomarkers that provide information about the injury mechanisms of CTE.

How can the challenges to conducting neuropathology research studies on the brain be met?

A fundamental goal of CTE research is to understand how impacts to the head cause symptomatic changes in brain function. Research efforts that are currently siloed could meet this goal more rapidly through coordinated efforts across institutions, according to Michael McCrea, Ph.D., Professor in the Department of Neurosurgery at the Medical College of Wisconsin. Already existing frameworks, such as the NINDS-led Common Data Elements Project, and data repository platforms, such as the Federal Interagency Traumatic Brain Injury Research (FITBIR) Informatics System and the Research Electronic Data Capture (REDCap), have potential to make multicenter collaborations effective by providing a robust search engine, standardization of laboratory methods and cross validation of findings.

A large study of many persons who were exposed to repetitive head injury but have died for other reasons would expand our knowledge of the prevalence of CTE and the risk factors for its development. Recruitment of brain donors with histories of repeated head injury, operational logistics, and standardization of protocols for harvesting and preserving specimens are challenges facing brain banks, according to H. Ronald Zielke, Ph.D., Director of the National Institute of Child Health and Human Development (NICHD) Brain and Tissue Bank for Developmental Disorders at the University Maryland School of Medicine. Nearly 35,000 tissue samples have been collected by the NICHD brain bank to date, and more than 800 researchers in 23 countries have evaluated the specimens.

Despite the large number of tissue samples in this bank, the number of cases with CTE is unknown because information about previous concussions or TBIs is lacking. The Sports Legacy Institute (SLI), co-founded in 2007 by Christopher Nowinski, currently a doctoral candidate at Boston University School of Medicine and a former Harvard University football player and professional wrestler, has facilitated the investigation of more than 140 brains, largely from former athletes. Nowinski emphasized the importance of building personal connections with the donors and their families and SLI has enlisted the support of the NFL Players Association in a campaign to recruit football players. To accelerate

neuropathology research, Roger Little, Ph.D., the National Institute of Mental Health, outlined plans to create the Neurobiobank, which will coordinate several NIH-funded brain banks across the U.S. to increase the availability of specimens for research and to stimulate interest in brain donation for scientific studies.

Questions for CTE Research

The workshop stimulated a great deal of discussion and a number of key research questions to inform the research community and the Federal agencies in advancing our understanding of CTE, its risk factors, how to diagnose it and how to better prevent and treat the disorder.

- What are the population prevalence and incidence of CTE?
- What are the number of impacts to the head and their magnitude that cause CTE?
- Is participation in contact sports a CTE risk factor for school-aged children and young adults?
- Is exposure to single or multiple blast exposures a risk factor for CTE in returning service members?
- Are there genetic susceptibilities to CTE?
- How can CTE be diagnosed in living people?
- Can PET studies using novel tau ligands detect CTE in living persons?
- Are CTE and single exposure TBI distinct pathologic processes or part of a disease spectrum?
- What neuropathology protocols should be followed to define minimal sampling requirements for CTE in a large autopsy-based study?
- What retrospective and prospective screening protocols should be followed to facilitate identification of potential CTE cases in brain banks?
- What are the relevant animal models of CTE pathology, especially TBI-related tau abnormalities?

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